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* * * * * Welcome to STN International * * * * *

NEWS	1		Web Page for STN Seminar Schedule - N. America
NEWS	2	AUG 06	CAS REGISTRY enhanced with new experimental property tags
NEWS	3	AUG 06	FSTA enhanced with new thesaurus edition
NEWS	4	AUG 13	CA/Capplus enhanced with additional kind codes for granted patents
NEWS	5	AUG 20	CA/Capplus enhanced with CAS indexing in pre-1907 records
NEWS	6	AUG 27	Full-text patent databases enhanced with predefined patent family display formats from INPADOCDB
NEWS	7	AUG 27	USPATOLD now available on STN
NEWS	8	AUG 28	CAS REGISTRY enhanced with additional experimental spectral property data
NEWS	9	SEP 07	STN AnaVist, Version 2.0, now available with Derwent World Patents Index
NEWS	10	SEP 13	FORIS renamed to SOFIS
NEWS	11	SEP 13	INPADOCDB enhanced with monthly SDI frequency
NEWS	12	SEP 17	CA/Capplus enhanced with printed CA page images from 1967-1998
NEWS	13	SEP 17	CAplus coverage extended to include traditional medicine. patents
NEWS	14	SEP 24	EMBASE, EMBAL, and LEMBASE reloaded with enhancements
NEWS	15	OCT 02	CA/Capplus enhanced with pre-1907 records from Chemisches Zentralblatt
NEWS	16	OCT 19	BEILSTEIN updated with new compounds
NEWS	17	NOV 15	Derwent Indian patent publication number format enhanced
NEWS	18	NOV 19	WPIX enhanced with XML display format
NEWS	19	NOV 30	ICSD reloaded with enhancements
NEWS	20	DEC 04	LINPADOCDB now available on STN
NEWS	21	DEC 14	BEILSTEIN pricing structure to change
NEWS	22	DEC 17	USPATOLD added to additional database clusters
NEWS	23	DEC 17	IMSDRUGCONF removed from database clusters and STN
NEWS	24	DEC 17	DGENE now includes more than 10 million sequences
NEWS	25	DEC 17	TOXCENTER enhanced with 2008 MeSH vocabulary in MEDLINE segment
NEWS	26	DEC 17	MEDLINE and LMEDLINE updated with 2008 MeSH vocabulary
NEWS	27	DEC 17	CA/Capplus enhanced with new custom IPC display formats
NEWS	28	DEC 17	STN Viewer enhanced with full-text patent content from USPATOLD
NEWS	29	JAN 02	STN pricing information for 2008 now available
NEWS	30	JAN 16	CAS patent coverage enhanced to include exemplified prophetic substances
NEWS	31	JAN 28	USPATFULL, USPAT2, and USPATOLD enhanced with new custom IPC display formats
NEWS	32	JAN 28	MARPAT searching enhanced
NEWS	33	JAN 28	USGENE now provides USPTO sequence data within 3 days of publication
NEWS	34	JAN 28	TOXCENTER enhanced with reloaded MEDLINE segment
NEWS	35	JAN 28	MEDLINE and LMEDLINE reloaded with enhancements

NEWS EXPRESS 19 SEPTEMBER 2007: CURRENT WINDOWS VERSION IS V8.2,

CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
AND CURRENT DISCOVER FILE IS DATED 19 SEPTEMBER 2007.

NEWS HOURS STN Operating Hours Plus Help Desk Availability
NEWS LOGIN Welcome Banner and News Items
NEWS IPC8 For general information regarding STN implementation of IPC 8

Enter NEWS followed by the item number or name to see news on that specific topic.

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* * * * * STN Columbus * * * * *

FILE 'HOME' ENTERED AT 13:06:24 ON 04 FEB 2008

=> file reg

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

0.84

0.84

FILE 'REGISTRY' ENTERED AT 13:08:35 ON 04 FEB 2008

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DICTIONARY FILE UPDATES: 3 FEB 2008 HIGHEST RN 1001389-12-3

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TSCA INFORMATION NOW CURRENT THROUGH June 29, 2007

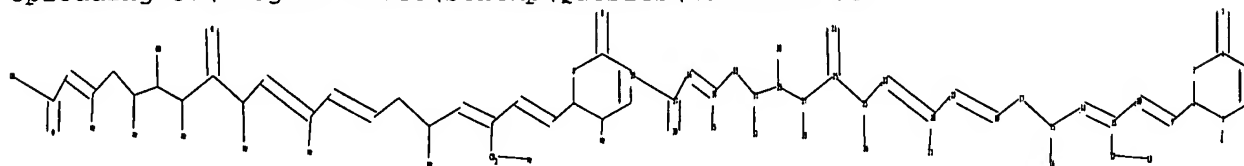
Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

<http://www.cas.org/support/stngen/stndoc/properties.html>

=>

Uploading C:\Program Files\Stnexp\Queries\10535672.str



chain nodes :

7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28
29 30 31 32 33 34 35 36 37 38 39

```

ring nodes :
1  2  3  4  5  6
chain bonds :
1-8  2-9  4-7  9-10  10-11  11-12  11-14  12-13  14-15  15-16  15-17  17-18  18-19
19-20  20-21  20-22  22-23  23-24  23-25  25-26  25-27  27-28  27-29  29-30  29-31
31-32  31-33  33-34  34-35  34-36  36-37  37-38  37-39
ring bonds :
1-2  1-6  2-3  3-4  4-5  5-6
exact/norm bonds :
4-7  25-26  29-30
exact bonds :
1-2  1-6  1-8  2-3  2-9  3-4  4-5  5-6  9-10  10-11  11-12  11-14  12-13  14-15
15-16  15-17  17-18  18-19  19-20  20-21  20-22  22-23  23-24  23-25  25-27  27-28
27-29  29-31  31-32  31-33  33-34  34-35  34-36  36-37
normalized bonds :
37-38  37-39
isolated ring systems :
containing 1 :

```

```

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:CLASS
11:CLASS 12:CLASS 13:CLASS 14:CLASS 15:CLASS 16:CLASS 17:CLASS 18:CLASS
19:CLASS 20:CLASS 21:CLASS 22:CLASS 23:CLASS 24:CLASS 25:CLASS 26:CLASS
27:CLASS 28:CLASS 29:CLASS 30:CLASS 31:CLASS 32:CLASS 33:CLASS 34:CLASS
35:CLASS 36:CLASS 37:CLASS 38:CLASS 39:CLASS

```

L1 STRUCTURE UPLOADED

=> d l1

L1 HAS NO ANSWERS

L1 STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.

=> s l1

SAMPLE SEARCH INITIATED 13:09:01 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED - 4 TO ITERATE

100.0% PROCESSED 4 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
 BATCH **COMPLETE**
PROJECTED ITERATIONS: 4 TO 200
PROJECTED ANSWERS: 0 TO 0

L2 0 SEA SSS SAM L1

=> s l1 full

FULL SEARCH INITIATED 13:09:06 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED - 69 TO ITERATE

100.0% PROCESSED 69 ITERATIONS 7 ANSWERS
SEARCH TIME: 00.00.01

L3 7 SEA SSS FUL L1

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	178.36	179.20

FILE 'CAPLUS' ENTERED AT 13:09:26 ON 04 FEB 2008
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 FILE LAST UPDATED: 3 Feb 2008 (20080203/ED)

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=> s 13 full
 L4 144 L3

=> file reg		
COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	0.48	179.68

FILE 'REGISTRY' ENTERED AT 13:09:47 ON 04 FEB 2008
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<http://www.cas.org/support/stngen/stndoc/properties.html>

=> s 13
 SAMPLE SEARCH INITIATED 13:09:51 FILE 'REGISTRY'
 SAMPLE SCREEN SEARCH COMPLETED - 4 TO ITERATE

100.0% PROCESSED 4 ITERATIONS
SEARCH TIME: 00.00.01

0 ANSWERS

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
 BATCH **COMPLETE**
PROJECTED ITERATIONS: 4 TO 200
PROJECTED ANSWERS: 0 TO 0

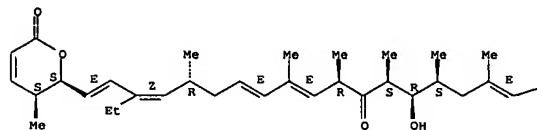
L5 0 SEA SSS SAM L1

=> d scan 13

L3 7 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STN
 IN 2,10,12,16,19-Nonadecapentaenoic acid,
 19-[(2S,3S)-3,6-dihydro-3-methyl-6-
 oxo-2H-pyran-2-yl]-17-ethyl-6-hydroxy-3,5,7,9,11,15-hexamethyl-8-oxo-,
 monosodium salt, (2E,5S,6R,7S,9R,10E,12E,15R,16Z,18E)- (9CI)
 MF C33 H48 O6 . Na

Absolute stereochemistry.
 Double bond geometry as shown.

PAGE 1-A



● Na

PAGE 1-B

CO₂H

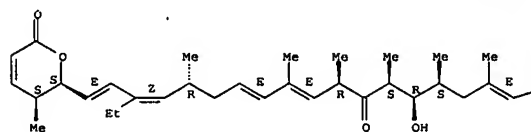
HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1

L3 7 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STN
 IN 2,10,12,16,18-Nonadecapentaenoic acid, 19-[(3,6-dihydro-3-methyl-6-oxo-2H-
 pyran-2-yl)-17-ethyl-6-hydroxy-3,5,7,9,11,15-hexamethyl-8-oxo-, compd.
 with N,N-diethylethanamine (1:1) (9CI)
 MF C33 H48 O6 . C6 H15 N

CM 1

Absolute stereochemistry.
 Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

CO₂H

CM 2

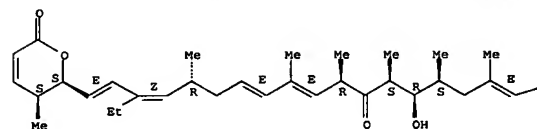


HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1

L3 7 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STN
 IN 2,10,12,16,18-Nonadecapentaenoic acid,
 19-[(2S,3S)-3,6-dihydro-3-methyl-6-
 oxo-2H-pyran-2-yl]-17-ethyl-6-hydroxy-3,5,7,9,11,15-hexamethyl-8-oxo-,
 (2E,5S,6R,7S,9R,10E,12E,15R,16Z,18E)-
 MF C33 H48 O6
 CI COM

Absolute stereochemistry.
 Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

CO₂H

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

=> file caplus		
COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	3.68	183.36

FILE 'CAPLUS' ENTERED AT 13:14:43 ON 04 FEB 2008
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 FILE LAST UPDATED: 3 Feb 2008 (20080203/ED)

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```
=> s 13 full
L6      144 L3

=> s 16 and leptomycin?
        647 LEPTOMYCIN?
L7      136 L6 AND LEPTOMYCIN?

=> s 17 and metalloproteinase?
        29028 METALLOPROTEINASES?
L8      2 L7 AND METALLOPROTEINASES?

=> s 17 and leptomycin B
        645 LEPTOMYCIN
        11 LEPTOMYCINS
        646 LEPTOMYCIN
            (LEPTOMYCIN OR LEPTOMYCINS)
        1750615 B
        618 LEPTOMYCIN B
            (LEPTOMYCIN(W)B)
L9      136 L7 AND LEPTOMYCIN B

=> s 19 and py<2002
        21937595 PY<2002
L10     55 L9 AND PY<2002

=> s 110 and skin
        272623 SKIN
        10809 SKINS
        278708 SKIN
            (SKIN OR SKINS)
L11     0 L10 AND SKIN
```

```
=> s l10 and fungal
      56895 FUNGAL
      15 FUNGALS
      56902 FUNGAL
          (FUNGAL OR FUNGALS)
L12      1 L10 AND FUNGAL

=> d ibib abs hitstr tot
```

ACCESSION NUMBER: 1998:94109 CAPLUS
DOCUMENT NUMBER: 128:215353
TITLE: Microbial conversion products of leptomycin B
AUTHOR(S): Kuhn, Michaela; Bitsch, Francis; Ponelle, Monique; Senglier, Jean-Jacques; Wang, Ying; Wolff, Barbara
CORPORATE SOURCE: Core Technology Area, Research, Novartis Pharma Inc., Basel, CH-4002, Switz.
SOURCE: Applied and Environmental Microbiology (1998), 64(2), 714-720
CODEN: AEMIDP; ISSN: 0099-2240
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 128:215353

AB Leptomycin B (LMB), a secondary metabolite produced by *Streptomyces* sp. strain ATC 1287 with known antifungal and antitumor effects, inhibits the nucleo-cytoplasmic translocation of the human immunodeficiency virus type 1 regulatory protein Rev and exhibits significant antiproliferative activity. Since LMB itself turned out to

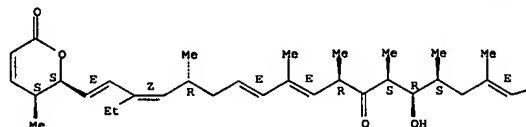
be distinctly cytotoxic, a bioconversion screening with a selected set of 29 bacterial and 72 fungal strains was performed in order to obtain metabolites of LMB with reduced antiproliferative effects. Several derivs. of LMB, more polar than the parent compound and produced in yields of >5%, were detected. Liquid chromatog.-mass spectroscopy anal.

indicated the type of bioconversion. Ferms. (1 L scale) of those strains with high rates of transformation were suitable for isolation and characterization of the most prominent metabolites. Thus, bioconversion of LMB with *Aspergillus flavus* ATCC 9170 and *Emericella unguis* ATCC 13431 served for isolation of the novel derivs. 26-hydroxy-LMB (30% was the concentration of the metabolite [with respect to LMB] used for bioconversion) and LMB-24-glutaminamide (90%), resp. *Streptomyces rimosus* ATCC 28893 converted LMB into 4,11-dihydroxy-LMB (13%) and 2,3-dihydro-LMB (55%). Although the antiproliferative effects of the LMB metabolites could be reduced through microbial conversion, none of these metabolites inhibited the nuclear export of Rev better than LMB itself.

IT 87081-35-4, Leptomycin B
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence) (microbial leptomycin B metabolites as proliferation inhibitors)
RN 87081-35-4 CAPLUS
CN 2,10,12,16,18-Nonadecapentaenoic acid, 19-[(2S,3S)-3,6-dihydro-3-methyl-6-oxo-2H-pyran-2-yl]-17-ethyl-6-hydroxy-3,5,7,9,11,15-hexamethyl-8-oxo-, (2E,5S,6R,7S,9R,10E,12E,15R,16Z,18E)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



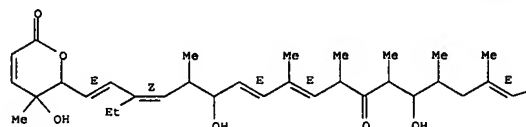
PAGE 1-B

CO₂H

IT 204330-96-1, 4,11-Dihydroxyleptomycin B
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence) (microbial leptomycin B metabolites as proliferation inhibitors)
RN 204330-96-1 CAPLUS
CN 2,10,12,16,18-Nonadecapentaenoic acid, 19-[(3,6-dihydro-3-hydroxy-3-methyl-6-oxo-2H-pyran-2-yl)-17-ethyl-6,14-dihydroxy-3,5,7,9,11,15-hexamethyl-8-oxo- (9CI) (CA INDEX NAME)

Double bond geometry as shown.
Currently available stereo shown.

PAGE 1-A



PAGE 1-B

CO₂H

REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

```
=> s l10 and tumor
      438664 TUMOR
      165222 TUMORS
      489727 TUMOR
              (TUMOR OR TUMORS)
L13      7 L10 AND TUMOR
=> d ibib abs hitstr tot
```

ACCESSION NUMBER: 2001:829425 CAPLUS
 DOCUMENT NUMBER: 136:80081
 TITLE: Dynamics of leptomycin B-sensitive nucleocytoplasmic flux of parathyroid hormone-related protein
 AUTHOR(S): Lam, Mark H. C.; Henderson, Beric; Gillespie, Matthew T.; Jans, David A.
 CORPORATE SOURCE: Nuclear Signalling Laboratory, Division of Biochemistry and Molecular Biology, John Curtin School
 of Medical Research, Canberra, Australia
 SOURCE: Traffic (Copenhagen, Denmark) (2001), 2(11), 812-819
 CODEN: TRAFFA; ISSN: 1398-9219
 PUBLISHER: Munksgaard International Publishers Ltd.
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB Parathyroid hormone-related protein is responsible for hypercalcemia induced by various tumors. The similarity of its N-terminus to that of parathyroid hormone enables parathyroid hormone-related protein to share parathyroid hormone's signaling properties, but the rest of the mol.

possesses distinct functions including a role in the nucleus/nucleolus in reducing apoptosis and enhancing cell proliferation. We have previously shown that parathyroid hormone-related protein nuclear import is mediated by importin β 1. Here we use fluorescence recovery after photobleaching for the first time to show that, in living cells, parathyroid hormone-related protein is exported from the nucleus in a leptomycin B-sensitive manner, implicating CRM1 as the parathyroid hormone-related protein nuclear export receptor. Leptomycin B treatment significantly reduced the rate of nuclear export 4-10-fold, thereby increasing parathyroid hormone-related protein concentration in the nucleus/nucleolus about 2-fold.

Intriguingly, this also led to a 2-fold reduced nuclear import rate. Inhibiting the nuclear export of a protein able to shuttle between nucleus and cytoplasm through distinct receptors thus can also affect nuclear import, indicating that the subcellular localization of a protein containing distinct nuclear

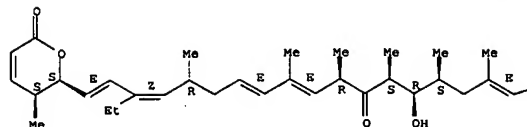
import and export signals is the product of an integrated system. Although there have been several recent studies examining the dynamics of intranuclear transport using fluorescence recovery after photobleaching, this represents, to our knowledge, the first use of the technique to examine the kinetics of nucleocytoplasmic flux in living cells.

IT 87081-35-4, Leptomycin B
 RL: BSU (Biological study, unclassified); BIOL (Biological study) (parathyroid hormone-related protein leptomycin B -sensitive nucleocytoplasmic flux and dynamics thereof)

RN 87081-35-4 CAPLUS
 CN 2,10,12,16,18-Nonadecapentaenoic acid,
 19-[(2S,3S)-3,6-dihydro-3-methyl-6-oxo-2H-pyran-2-yl]-17-ethyl-6-hydroxy-3,5,7,9,11,15-hexamethyl-8-oxo-, (2E,5S,6R,7S,9R,10E,12E,15R,16Z,18E)- (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

CO₂H

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

ACCESSION NUMBER: 2001:815253 CAPLUS
 DOCUMENT NUMBER: 136:49258
 TITLE: Suppressor of fused negatively regulates β -catenin signaling
 AUTHOR(S): Meng, Xianwang; Poon, Raymond; Zhang, Xiaoyun; Cheah, Alexander; Ding, Qi; Hui, Chi-Chung; Alman, Benjamin
 CORPORATE SOURCE: Program in Developmental Biology, The Hospital for Sick Children, University of Toronto, Toronto, ON, M5G1X8, Can.
 SOURCE: Journal of Biological Chemistry (2001), 276(43), 40113-40119
 CODEN: JBCHA3; ISSN: 0021-9258
 PUBLISHER: American Society for Biochemistry and Molecular Biology
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Suppressor of fused (Su(fu)) is a neg. regulator of the Hedgehog signaling

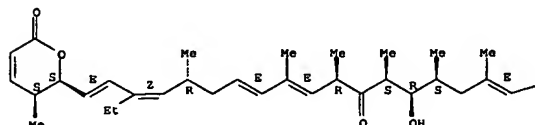
pathway that controls the nuclear-cytoplasmic distribution of Gli/Ci transcription factors through direct protein-protein interactions. We show here that Su(fu) is present in a complex with the oncogenic transcriptional activator β -catenin and functions as a neg. regulator of T-cell factor (Tcf)-dependent transcription. Overexpression of Su(fu) in SW480 (APCmut) colon cancer cells in which β -catenin protein is stabilized leads to a reduction in nuclear β -catenin levels and in Tcf-dependent transcription. This effect of Su(fu) overexpression can be blocked by treatment of these cells with leptomycin B, a specific inhibitor of CRM1-mediated nuclear export. Overexpression of Su(fu) suppresses growth of SW480 (APCmut) tumor cells in nude mice. These observations indicate that Su(fu) neg. regulates β -catenin signaling and that CRM-1-mediated nuclear export plays a role in this regulation. Our results also suggest that Su(fu) acts as a tumor suppressor.

IT 87081-35-4, Leptomycin B
 RL: BSU (Biological study, unclassified); BIOL (Biological study) (suppressor of fused neg. regulates β -catenin signaling)

RN 87081-35-4 CAPLUS
 CN 2,10,12,16,18-Nonadecapentaenoic acid,
 19-[(2S,3S)-3,6-dihydro-3-methyl-6-oxo-2H-pyran-2-yl]-17-ethyl-6-hydroxy-3,5,7,9,11,15-hexamethyl-8-oxo-, (2E,5S,6R,7S,9R,10E,12E,15R,16Z,18E)- (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

CO₂H

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

L13 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2000:780361 CAPLUS

DOCUMENT NUMBER: 134:82300

TITLE: Adenomatous polyposis coli protein contains two nuclear export signals and shuttles between the nucleus and cytoplasm

AUTHOR(S): Neufeld, Kristi L.; Nix, David A.; Bogerd, Hal; Kang, Yibin; Beckerle, Mary C.; Cullen, Bryan R.; White, Raymond L.

CORPORATE SOURCE: Department of Oncological Sciences, Huntsman Cancer Institute, University of Utah, Salt Lake City, UT, 84112, USA

SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2000), 97(22), 12095-12099

CODEN: PNASAG; ISSN: 0027-8424

PUBLISHER: National Academy of Sciences

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Mutational inactivation of the adenomatous polyposis coli (APC) tumor suppressor initiates most hereditary and sporadic colon carcinomas. Although APC protein is located in both the cytoplasm and

nucleus, the protein domains required to maintain a predominantly cytoplasmic localization are unknown. Here, we demonstrate that nuclear export of APC is mediated by two intrinsic, leucine-rich, nuclear export signals (NESs) located near the amino terminus. Each NES was able to induce the nuclear export of a fused carrier protein. Both APC NESs were independently able to interact with the Crml nuclear export factor and substitute for the HIV-1 Rev NES to mediate nuclear mRNA export. Both

APC NESs functioned within the context of APC sequence: an amino-terminal APC peptide containing both NESs interacted with Crml and showed nuclear export in

a heterokaryon nucleocytoplasmic shuttling assay. Also, mutation of both APC NESs resulted in the nuclear accumulation of the full-length, approx.320-kDa APC protein, further establishing that the two intrinsic APC NESs are necessary for APC protein nuclear export. Moreover, endogenous APC accumulated in the nucleus of cells treated with the Crml-specific nuclear export inhibitor leptomycin B. Together, these data indicate that APC is a nucleocytoplasmic shuttle protein whose predominantly cytoplasmic localization requires NES function

and suggests that APC may be important for signaling between the nuclear and cytoplasmic compartments of epithelial cells.

IT 87081-35-4, Leptomycin B

RL: BAC (Biological activity or effector, except adverse); BSU

(Biological

study, unclassified); BIOL (Biological study) (nuclear export inhibitor leptomycin B blocks APC protein transport to cytoplasm)

RN 87081-35-4 CAPLUS

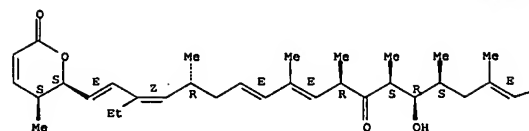
CN 2,10,12,16,18-Nonadecapentaenoic acid,

19-((2S,3S)-3,6-dihydro-3-methyl-6-oxo-2H-pyran-2-yl)-17-ethyl-6-hydroxy-3,5,7,9,11,15-hexamethyl-8-oxo-, (2E,5S,6R,7S,9R,10E,12E,15R,16Z,18E)- (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

L13 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2008 ACS on STN (Continued)

PAGE 1-A



PAGE 1-B

CO₂H

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS

FORMAT RECORD. ALL CITATIONS AVAILABLE IN THE RE

L13 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2000:525399 CAPLUS

DOCUMENT NUMBER: 133:217377

TITLE: Activation of p53 in cervical carcinoma cells by small

small molecules

AUTHOR(S): Hietanen, Sakari; Lain, Sonia; Krausz, Eberhard; Blattner, Christine; Lane, David P.

CORPORATE SOURCE: CRC Cell Transformation Group, Department of Biochemistry, University of Dundee, Dundee, DD1 5EH, UK

SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2000), 97(15), 8501-8506

CODEN: PNASAG; ISSN: 0027-8424

PUBLISHER: National Academy of Sciences

DOCUMENT TYPE: Journal

LANGUAGE: English

AB In over 90% of cervical cancers and cancer-derived cell lines, the p53 tumor suppressor pathway is disrupted by human papillomavirus (HPV). The HPV E6 protein promotes the degradation of p53 and thus

inhibits the stabilization and activation of p53 that would normally occur in response to HPV E7 oncogene expression. Restoration of p53 function in these cells by blocking this pathway should promote a selective therapeutic effect. Here we show that treatment with the small mol. nuclear export inhibitor, leptomycin B, and

actinomycin D leads to the accumulation of transcriptionally active p53 in the nucleus of HeLa, CaSki, and SiHa cells. Northern blot analyses showed

that both actinomycin D and leptomycin B reduced the amount of HPV E6-E7 mRNA whereas combined treatment with the drugs showed almost complete disappearance of the viral mRNA. The combined treatment activated p53-dependent transcription, and increases in both p21WAF1/CIP1 and Hdm2 mRNA were seen. The combined treatment resulted in apoptotic death in the cells, as evidenced by nuclear fragmentation and PARP-cleavage indicative of caspase 3 activity. These effects were greatly reduced by expressing a dominant neg. p53 protein. The present study shows that small mols. can reactivate p53 in cervical carcinoma cells, and this reactivation is associated with an extensive biol.

response, including the induction of the apoptotic death of the cells.

IT 87081-35-4, Leptomycin B

RL: BAC (Biological activity or effector, except adverse); BSU

(Biological

study, unclassified); THU (Therapeutic use); BIOL (Biological study);

USES

(activation of p53 in cervical carcinoma cells by small mols.)

RN 87081-35-4 CAPLUS

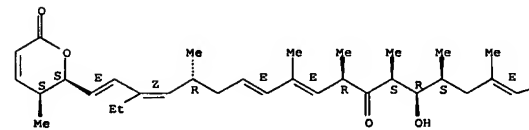
CN 2,10,12,16,18-Nonadecapentaenoic acid,

19-((2S,3S)-3,6-dihydro-3-methyl-6-oxo-2H-pyran-2-yl)-17-ethyl-6-hydroxy-3,5,7,9,11,15-hexamethyl-8-oxo-, (2E,5S,6R,7S,9R,10E,12E,15R,16Z,18E)- (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry as shown.

L13 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2008 ACS on STN (Continued)

PAGE 1-A



PAGE 1-B

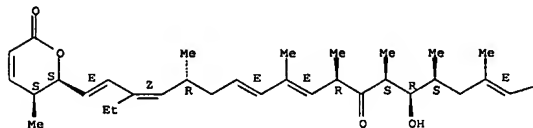
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REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS

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L13 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 2000:9882 CAPLUS
 DOCUMENT NUMBER: 132:146316
 TITLE: Effects on normal fibroblasts and neuroblastoma cells of the activation of the p53 response by the nuclear export inhibitor leptomycin B
 AUTHOR(S): Smart, Philip; Lane, E. Birgitte; Lane, David P.; Winkley, Carol; Vojtesek, Borek; Lain, Sonia
 CORPORATE SOURCE: CRC Cell Transformation Group, Department of Biochemistry, MSI/WTB, University of Dundee, Dundee, DD1 5EH, UK
 SOURCE: Oncogene (1999), 18(51), 7378-7386
 CODEN: ONCNE5; ISSN: 0950-9232
 PUBLISHER: Stockton Press
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB P53 tumor suppressor protein levels and p53-dependent transcriptional activity have been recently shown to increase in cells treated with leptomycin B (LMB), an inhibitor of nuclear export. Expts. presented here show that LMB treatment leads to growth arrest and a senescence-like phenotype in human normal fibroblast cultures. This effect is reversible after removal of the drug and further passage by trypsinization. Instead, LMB has a strong cytotoxic effect on human neuroblastoma cell lines even at nanomolar concns. In both these cell types the effects of LMB are attenuated when the activity of the endogenous wild type p53 protein is abrogated by overexpression of a dominant neg. p53 mutant. We conclude that the induction of the p53 response by LMB plays an important role in the effects of this drug on cultured cells.
 IT 87081-35-4, Leptomycin B
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study (effects of activation of the p53 response by leptomycin B on normal fibroblasts and neuroblastoma cells))
 RN 87081-35-4 CAPLUS
 CN 2,10,12,16,18-Nonadecapentaenoic acid,
 19-[(2S,3S)-3,6-dihydro-3-methyl-6-oxo-2H-pyran-2-yl]-17-ethyl-6-hydroxy-3,5,7,9,11,15-hexamethyl-8-oxo-,
 (2E,5S,6R,7S,9R,10E,12E,15R,16Z,18E)- (CA INDEX NAME)
 Absolute stereochemistry.
 Double bond geometry as shown.

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L13 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2008 ACS on STN (Continued)

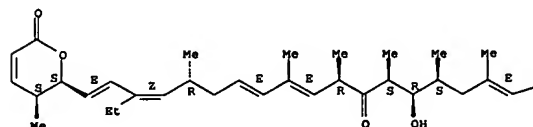
PAGE 1-B

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REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
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L13 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 1987:451496 CAPLUS
 DOCUMENT NUMBER: 107:51496
 TITLE: Studies on the new antibiotics kazusamycin and related substances
 AUTHOR(S): Umezawa, Iwao; Komiyama, Kanji
 CORPORATE SOURCE: Kitesato Inst., Japan
 SOURCE: Gan to Kagaku Ryoho (1987), 14(3, Pt. 2), 858-64
 CODEN: GTRDX; ISSN: 0385-0684
 DOCUMENT TYPE: Journal
 LANGUAGE: Japanese
 AB Kazusamycins A and B and leptomycin B have a structure characteristic of an unsatd., branched-chain fatty acid with a terminal δ-lactone ring, and the former 2 agents show antimicrobial activity on some kinds of fungi. Kazusamycin A (KZM-A) showed cytotoxic activity on mammalian cells at very low concns. (nanogram per ml range) in vitro. The antibiotic inhibited not only the growth of transplantable murine tumors and their metastases to the lung but also human mammary tumors inoculated into nude mice. KZM-A was rapidly distributed to the main organs of mice, and a percentage of the antibiotic was inactivated by binding to high-mol.-weight substances such as albumin. A large quantity of KZM-A was carried to the liver and excreted into the bile, but was then reabsorbed by the small intestine. The growth of tumor metastases (LS178Y cells) in the liver was suppressed by KZM-A. The antibiotic induced severe diarrhea by causing necrosis and/or lysis of the mucous membrane of the small intestine. In contrast to this, the degree of myelotoxicity was relatively slight. The active site of the fatty acid of KZM-A appeared to consist of conjugated double bonds, carboxylic acid, and hydroxyl moieties.
 IT 87081-35-4, Leptomycin B
 RL: PRP (Properties) (antimicrobial and antitumor effects of)
 RN 87081-35-4 CAPLUS
 CN 2,10,12,16,18-Nonadecapentaenoic acid,
 19-[(2S,3S)-3,6-dihydro-3-methyl-6-oxo-2H-pyran-2-yl]-17-ethyl-6-hydroxy-3,5,7,9,11,15-hexamethyl-8-oxo-,
 (2E,5S,6R,7S,9R,10E,12E,15R,16Z,18E)- (CA INDEX NAME)
 Absolute stereochemistry.
 Double bond geometry as shown.

PAGE 1-A



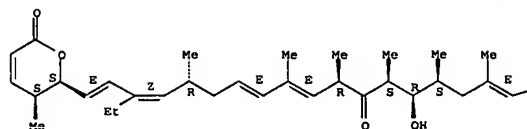
L13 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2008 ACS on STN (Continued)

PAGE 1-B

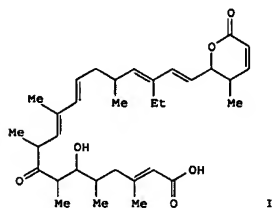
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ACCESSION NUMBER: 1985:214721 CAPLUS
 DOCUMENT NUMBER: 102:214721
 ORIGINAL REFERENCE NO.: 102:33527a,33530a
 TITLE: Antitumor activity of leptomycin B
 AUTHOR(S): Komiyama, Kanki; Okada, Kenji; Tomisaka, Shigeru;
 Umezawa, Iwao; Hanamoto, Tetsuo; Beppu, Teruhiko
 CORPORATE SOURCE: KITASATO Inst., Tokyo, 108, Japan
 SOURCE: Journal of Antibiotics (1985), 38(3), 427-9
 CODEN: JANTAJ; ISSN: 0021-8820
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 GI

PAGE 1-A



PAGE 1-B



1

AB Leptomycin B (1) [87081-35-4] increased the life span of mice bearing Erlich ascites tumors and Lewis lung carcinoma, but had only slight effects in mice bearing B-16 melanoma and P-388 lymphatic leukemia. 1 inhibited the growth of HeLa cells at a concentration of 4.9 ng/mL when the cells were exposed for 3 days. When

HeLa cells were exposed to 1 for 3 days, many polynuclear giant cells and masses of small nuclei appeared at a concentration of 1.25-2.5 ng/mL. Thus, the

antitumor activity of 1 appears to be due to a direct cytotoxic activity. IT 87081-35-4

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES

(Uses) (neoplasm inhibition by, mechanism of)

RN 87081-35-4 CAPLUS

CN 2,10,12,16,18-Nonadecapentaenoic acid,

19-[(2S,3S)-3,6-dihydro-3-methyl-6-oxo-2H-pyran-2-yl]-17-ethyl-6-hydroxy-3,5,7,9,11,15-hexamethyl-8-oxo-, (2E,5S,6R,7S,9R,10E,12E,15R,16Z,18E)- (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.

CO₂H

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COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
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FULL ESTIMATED COST

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE	TOTAL
ENTRY	SESSION
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FILE CONTAINS CURRENT INFORMATION.
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FILE 'REGISTRY' ENTERED AT 13:08:35 ON 04 FEB 2008

L1 STRUCTURE UPLOADED
L2 0 S L1
L3 7 S L1 FULL

FILE 'CAPLUS' ENTERED AT 13:09:26 ON 04 FEB 2008

L4 144 S L3 FULL

FILE 'REGISTRY' ENTERED AT 13:09:47 ON 04 FEB 2008

L5 0 S L3

FILE 'CAPLUS' ENTERED AT 13:14:43 ON 04 FEB 2008

L6 144 S L3 FULL
L7 136 S L6 AND LEPTOMYCIN?
L8 2 S L7 AND METALLOPROTEINAS?
L9 136 S L7 AND LEPTOMYCIN B
L10 55 S L9 AND PY<2002
L11 0 S L10 AND SKIN
L12 1 S L10 AND FUNGAL
L13 7 S L10 AND TUMOR

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COST IN U.S. DOLLARS

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FULL ESTIMATED COST

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE	TOTAL
ENTRY	SESSION
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